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-- A method is disclosed for determining whether a compound binds to a lipoprotein such as LDL or VLDL in a manner which will lower plasma cholesterol. The method provided includes assessing the ability of the compound to form a complex with the lipoprotein, and then determining whether the newly formed complex causes a change in the structure of apoB-100 that results in increased binding affinity to an LDL receptor.--

### **Information Disclosure Statement**

A full translation of French Patent No. 2.168.137 which is the most representative of the French patent documents AQ-AV listed on the original information disclosure statement is provided on the attached supplemental Information Disclosure Statement (PTO Form 1449).

### **In the Claims**

Applicants amend claims 1, 4-6, 9, 15, 21-24, 25, 26 and 29-36. Applicants provide the text of the amended claims below and then attach a marked-up version of the original claims that indicates the amendments.

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1. (Twice Amended) A method to assess whether a compound first binds to and then enhances the clearing of a cholesterol-containing low density lipoprotein (LDL) after subsequent binding to the low density lipoprotein receptor in a host human or other animal comprising:

- (a) administering the compound to the host,
- (b) isolating the cholesterol-containing low density lipoprotein from the host,

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(c) determining whether the binding of the compound to the cholesterol-containing low density lipoprotein forms a complex; and

(d) determining whether the complex results in a change in the three dimensional conformation of the lipoprotein that enhances the binding affinity of the lipoprotein to the low density lipoprotein receptor.

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4. (Amended) The method of claim 1, wherein the binding of the compound to the cholesterol-containing low density lipoprotein is assessed by a sandwich immunoreactivity assay.

5. (Amended) The method of claim 1, wherein the binding of the compound to the cholesterol-containing low density lipoprotein is assessed using agarose electrophoresis.

6. (Twice Amended) A method to determine whether a compound first binds to and then increases the clearance of a low density lipoprotein after subsequent binding to the low density lipoprotein receptor in a host, comprising

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(i) mixing the compound with low density lipoprotein;

(ii) determining whether the compound binds to the low density lipoprotein and forms a complex; and

(iii) determining whether the complex alters the three dimensional conformation of the lipoprotein such that the binding of the lipoprotein to a lipoprotein receptor is enhanced.

9. (Twice Amended) A method to determine if a compound causes a change in the structure of apolipoprotein B-100 in a cholesterol-containing low density lipoprotein, wherein, an epitope on the apolipoprotein B-100 binds to an LDL-receptor, comprising:

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- (i) mixing the compound with and allowing it to bind to low density lipoprotein;
  - (ii) carrying out a sandwich immunoreactivity assay on the compound-low density lipoprotein mixture using a first antibody directed to the epitope on apolipoprotein B-100 that binds to the LDL-receptor,
  - (iii) using a second, capture antibody that is attached to a solid phase and which binds to the first antibody;
  - (iv) detecting the second capture antibody bound to the first antibody
  - (v) quantifying the amount of the first antibody - LDL - compound captured by the second antibody; and
  - (vi) comparing the amount of LDL captured by the assay to a control.

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15. (Twice Amended) A method for assessing whether a compound first binds to a lipoprotein, enhancing the binding of the lipoprotein to a low density lipoprotein hepatic receptor and thus lowering plasma cholesterol, the method comprising:

- (a) allowing the compound to form a complex with a cholesterol-containing lipoprotein in vivo,
- (b) isolating the resulting complex, and

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(c) determining whether the formation of the complex causes a change in the three dimensional conformation of apoB-100 in the lipoprotein that enhances the binding of the lipoprotein to the LDL hepatic receptor.

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21. (Amended) The method of claim 2, wherein the apolipoprotein is apoB-100.

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22. (Amended) The method of claim 1, wherein the lipoprotein receptor is hepatic.

Sub-D5

23. (Amended) The method of claim 6, wherein the lipoprotein is VLDL.

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25. (Amended) The method of claim 6, wherein the determination of whether the compound binds to the low-density lipoprotein and forms a complex is assessed by a sandwich immunoreactivity assay.

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26. (Amended) The method of claim 6, wherein the determination of whether the compound binds to the low-density lipoprotein and forms a complex is assessed using agarose electrophoresis.

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29. (Amended) The method of claim 9, wherein the control is cholesterol-containing low density lipoprotein in the absence of test compound.

Sub-D6

30. (Amended) The method of claim 10, wherein the cholesterol-containing low-density lipoprotein is VLDL.

31. (Amended) The method of claim 15, wherein the formation of the complex is determined by a sandwich immunoreactivity assay.

32. (Amended) The method of claim 15, wherein the formation of the complex is determined using agarose electrophoresis.

~~33. (Amended) The method of claim 9, wherein the apolipoprotein is apoB-100.~~

~~34. (Amended) The method of claim 9, wherein the lipoprotein-receptor is a low-density lipoprotein (LDL) receptor.~~

Sub 27  
35. (Amended) The method of claim 15, wherein the cholesterol-containing low-density lipoprotein is LDL.

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36. (Amended) The method of claim 15, wherein the cholesterol-containing low-density lipoprotein is VLDL.